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GIFFORD, KRASS, SPRINKLE, ANDERSON &
CITKOWSKI, P.C.
P.O. BOX 7021
TROY, MI 48007-7021

EXAMINER	
BARNHART, LORA ELIZABETH	

ART UNIT	PAPER NUMBER
1651	

MAIL DATE	DELIVERY MODE
12/11/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/516,899	MEYTHALER ET AL.	
	Examiner	Art Unit	
	Lora E. Barnhart	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 September 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) *5-8,10,11,13-23,25-35 and 37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,9,12,24,36 and 38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/14/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-38 as originally filed are currently pending.

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-25, 36, and 38, in the reply filed on 9/17/08 is acknowledged. Applicant's further election of the species "a defibrinogenic agent" and "ancrod" in the same reply is acknowledged.

Claims 26-35 and 37 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 5-8, 10, 11, 13-23, and 25 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim.

Examination on the merits will commence at this time on claims 1-4, 9, 12, 24, 36, and 38 as they read on the elected species where appropriate. Claim 9 will be examined to the extent it reads on the elected species "ancrod," i.e., "wherein the defibrinogenic agent is a functional fragment of a natural or synthetic reptile peptide." See the rejection below under 35 U.S.C. § 112, second paragraph.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4, 9, 12, 24, 36, and 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 requires administering a clot-reducing agent to a subject "having preconditions." The scope of "preconditions" is not clear, since the claim does not particularly require that these preconditions be related to obstructive hydrocephalus or any disorder. The scope of the patient set is not clear. Clarification is required. Applicant is cautioned that amending the claim such that it reads on preventing obstructive hydrocephalus may necessitate a rejection under 35 U.S.C. § 112, first paragraph, as lacking enablement.

Claim 1 is drawn to a method of reducing cerebrospinal fluid flow obstruction the comprises maintaining "a therapeutic amount" of a clot-reducing agent within the subject being treated "for a period of time sufficient to reduce" the obstruction. These limitations are unclear because the person of ordinary skill in the art could not identify the amount or the period of time for all clot-reducing agents based on the limited disclosure in the specification. See M.P.E.P. § 2173.05(c), section III. It is further noted that the claim does not necessarily require that the subject have any CSF obstructions (the subject may have some unnamed "preconditions" that do not appear to necessarily include obstructed CSF), so identifying an amount of agent and therapeutic time could not be accomplished in these cases based on the limited guidance in the disclosure (see pages 9-10 of the as-filed specification). Clarification is required.

Because claims 2-4, 9, 12, and 24 depend from indefinite claim 1 and do not clarify these points of confusion, they must also be rejected under 35 U.S.C. 112, second paragraph.

Claim 3 is queried because it includes among the "devices" for administration "an injection," which is not a device per se. Clarification is required.

Claim 9 allows that the agent may be, inter alia, "a prodrug thereof." It is not clear to which element in the list this final "thereof" refers. Clarification is required. The species should be particularly and clearly recited.

Claim 12 allows that the agent may be ancrod or, inter alia, "a prodrug thereof." It is not clear to which element in the list this final "thereof" refers. Clarification is required. The species should be particularly and clearly recited.

Claims 36 and 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite in that it fails to point out what is included or excluded by the claim language. These claims are omnibus type claims, which are wholly incompatible with current U.S. practice. See M.P.E.P. § 2173.05(r). These claims should be canceled entirely or amended such that they particularly point out the scope of the method being claimed, preferably by reciting positive method steps. For the purpose of art rejections, these claims are interpreted as encompassing any step of any method discussed in the specification.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 36, and 38 are rejected under 35 U.S.C. 102(b) as being anticipated by Naff et al. (2000, *Stroke* 31: 841-847; reference U). This rejection addresses the embodiment drawn to a method of reducing cerebrospinal fluid flow obstruction by administering a therapeutic dose of urokinase, a clot-reducing agent, to a subject having obstructive hydrocephalus.

Naff teaches treating patients who require an intraventricular catheter (IVC) to treat obstructive hydrocephalus resulting from intraventricular hemorrhage (IVH) with ABBOKINASE, a preparation of urokinase (page 842, column 1, under “Criteria…” and “Treatment Protocol"). Naff teaches administering urokinase every 12 hours until the IVC is no longer necessary (page 842, column 2, paragraph 1). Naff teaches that patients so treated show a significant improvement in 30-day survival because the intracranial pressure (ICP) resulting from obstructive hydrocephalus is lessened (page 845 under “Discussion”). Urokinase is a defibrinogenic agent in that it is a thrombolytic agent, i.e., it dissolves fibrin blood clots (page 845, column 1).

Claims 1-4, 36, and 38 are rejected under 35 U.S.C. 102(b) as being anticipated by Wright et al. (2001, *Journal of Stroke and Cerebrovascular Diseases* 10: 23-26; reference V). This rejection addresses the embodiment drawn to a method of reducing cerebrospinal fluid flow obstruction by administering a therapeutic dose of urokinase, a clot-reducing agent, to a subject having obstructive hydrocephalus.

Wright teaches inserting an IVC into the brain of a patient with obstructive hydrocephalus, then administering 25,000 units of intraventricular urokinase every 12

hours, following an established protocol (page 24, column 1, last paragraph et seq.). Wright teaches that the urokinase reduced the size of the blood clot near the IVC insertion site (ibid.). Wright teaches repositioning the IVC to the site of additional blood clots and administering additional urokinase, thereby reducing the size of those additional clots (page24, column 2, paragraph 2). Wright teaches that the urokinase treatment resulted in prompt improvement in the patient's condition and no subsequent hydrocephalus ((ibid.). Wright teaches that an IVC alone does not dissolve the clot itself and that a combination of external ventricular drainage (EVD) and urokinase treatment caused rapid lysis of the clot and subsequent improvement in the patient's condition (page 25, column 2). Urokinase is a defibrinogenic agent in that it is a thrombolytic agent, i.e., it dissolves fibrin blood clots (page 23, column 2, e.g.).

Claims 1-4, 36, and 38 are rejected under 35 U.S.C. 102(e) as being anticipated by Hanley et al. (2006, U.S. Patent Application Publication 2006/0078555; reference A). This rejection addresses the embodiment drawn to a method of reducing cerebrospinal fluid flow obstruction by administering a therapeutic dose of urokinase or recombinant tissue plasminogen activator (rt-PA), clot-reducing agents, to a subject having obstructive hydrocephalus.

Hanley teaches treating patients who require an IVC to treat obstructive hydrocephalus resulting from IVH using EVD (paragraphs 92 and 96) with an injection of 25,000 units of urokinase or rt-PA every 12 hours through the IVC until the hydrocephalus was resolved (paragraphs 96-98 and 129). Hanley teaches that patients

treated with intraventricular thrombolytic agents showed marked improvement in obstructive hydrocephalus symptoms (paragraphs 120 and 133, e.g.). Urokinase and rt-PA are defibrinogenic agents in that they are thrombolytic agent, i.e., they dissolve fibrin blood clots (paragraph 68, e.g.).

Claims 1-4, 9, 12, 36, and 38 are rejected under 35 U.S.C. 102(b) as being anticipated by Schwartz et al. (1996, U.S. Patent 5,523,292; reference B). This rejection addresses the embodiment drawn to a method of reducing cerebrospinal fluid flow obstruction by administering a therapeutic dose of ancrod, a clot-reducing agent, to a subject having preconditions. It is noted that claim 1 does not describe the nature of these preconditions; therefore, any patient with preconditions may be the "subject" in the claimed method. Furthermore, none of the claims particularly limits the location of administration of the clot-reducing agent.

Schwartz teaches reducing restenosis in patients with a predisposition toward restenosis (i.e., a "precondition") by administering ancrod, a defibrinogenic snake venom protein (see Example at columns 3-5 and column 2, lines 9-11). While Schwartz does not teach reducing cerebrospinal fluid flow obstruction, they do perform the same administration of ancrod as in the present application. Because the method steps are the same, Schwartz inherently teaches the same process of reduction of cerebrospinal fluid flow obstruction as in the current application. Schwartz therefore anticipates reducing cerebrospinal fluid flow obstruction as instantly claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 9, 12, 24, 36, and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Naff et al. (2000, *Stroke* 31: 841-847) taken in view of Schwartz et al. (1996, U.S. Patent 5,523,292).

Naff teaches treating patients who require an intraventricular catheter (IVC) to treat obstructive hydrocephalus resulting from intraventricular hemorrhage (IVH) with ABBOKINASE, a preparation of urokinase (page 842, column 1, under “Criteria…” and “Treatment Protocol"). Naff teaches administering urokinase every 12 hours until the IVC is no longer necessary (page 842, column 2, paragraph 1). Naff teaches that patients so treated show a significant improvement in 30-day survival because the

intracranial pressure (ICP) resulting from obstructive hydrocephalus is lessened (page 845 under "Discussion"). Urokinase is a defibrinogenic agent in that it is a thrombolytic agent, i.e., it dissolves fibrin blood clots (page 845, column 1).

Naff does not teach treating obstructive hydrocephalus by administering a defibrinogenic agent that is a natural or synthetic reptile peptide, e.g. ancrod.

Schwartz teaches that ancrod is an defibrinogenic agent that dissolves blood clots (column 2, lines 32-41). Schwartz teaches that ancrod may be administered in various amounts for various times via various routes to prevent thrombus formation (column 2, line 43, through column 3, line 12).

A person of ordinary skill in the art would have had a reasonable expectation of success in substituting the ancrod of Schwartz for urokinase in the method of Naff because urokinase and ancrod are both explicitly taught as being useful as defibrinogenic agents that dissolve clots. Therefore, these compositions are functional equivalents in the art, and substituting one for the other would have been obvious at the time of the invention. "When a patent 'simply arranges old elements with each performing the same function it had been known to perform' and yields no more than one would expect from such an arrangement, the combination is obvious." See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007) at 1395-1396, quoting *Sakraida v. AG Pro, Inc.,* 425 U.S. 273 (1976).

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was made to substitute ancrod for urokinase in the method of Naff because the two agents were known in the art to be functional equivalents.

Therefore, the invention as a whole would have been *prima facie* obvious to a person of ordinary skill at the time the invention was made.

No claims are allowed. No claims are free of the art.

Applicant is requested to specifically point out the support for any amendments made to the disclosure in response to this Office action, including the claims (MPEP 714.02 and 2163.06). In doing so, applicant is requested to refer to pages and line numbers in the as-filed specification, **not** the published application. Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending U.S. applications that set forth similar subject matter to the present claims and share an inventor or assignee with the instant application. A copy of such copending claims is requested in response to this Office action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lora E. Barnhart whose telephone number is 571-272-1928. The examiner can normally be reached on Monday-Thursday, 9:00am - 5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lora E Barnhart/
Primary Examiner, Art Unit 1651